Developmental Biology 319 (2008) 544–546

Contents lists available at ScienceDirect

Developmental Biology

journal homepage: www.elsevier.com/developmentalbiology

Abstracts

Cell proliferation

Program/Abstract # 261

Withdrawn

doi:10.1016/j.ydbio.2008.05.278

Program/Abstract # 262

Maternal-effect brambleberry functions during cleavage stage to maintain nuclear integrity

Elliott W. Abrams, Florence Marlow, Lee Kapp, Tripti Gupta, Mary Mullins
University of Pennsylvania, Department of Cell and Developmental Biology, Philadelphia, PA, USA

Embryonic development in most animals initiates with a series of rapid and synchronous cell cleavages. Cleavage cycles are mediated by maternal factors present in the egg and are missing cell cycle checkpoints. Understanding how chromosome integrity is maintained during this very critical period of metazoan development is currently lacking. By performing a forward genetic screen in zebrafish, we recently identified a maternal-effect mutant, *brambleberry* (*bmb*), which exhibits profound chromatin defects during the cleavage stage of development. Interphase *bmb* nuclei appear as individual clusters of chromatin bodies and are sometimes associated with a few DAPI-stained microfragments. Examination of the mitotic spindle indicates that chromosomes are not properly aligned on the metaphase plate during mitosis. Interestingly, inspection of the nuclear envelope reveals that during interphase chromatin bodies appear individually encased in separate nuclear envelopes. Surprisingly, *bmb* nuclear morphology is greatly improved just after the mid-blastula transition (MBT), despite *bmb* mutants arresting development at this point. This effect is not diminished when both maternal and paternal functions of *bmb* are eliminated, suggesting that *bmb* functions specifically during the cleavage stage of embryonic development. Further characterization of *bmb* mutants involves examining other mitotic components and aspects of nuclear/chromatin structure. Finally, significant effort is being put forth into the positional cloning of the *bmb* gene to help elucidate its molecular function.

doi:10.1016/j.ydbio.2008.05.279

Program/Abstract # 263

Developmental regulation of cell division mechanisms in a vertebrate embryo

Esther Kieserman [a], Michael Glotzer [b], John B. Wallingford [a]
[a] *Department of Molecular Cell and Developmental Biology, ICMB, University of Texas at Austin, Austin, TX, USA*
[b] *Department of Molecular Genetics and Cell Biology, University of Chicago, Chicago, IL, USA*

Proper completion of cell division in organisms is critical for morphogenesis and embryogenesis. Comparatively little analysis has been made of core cytokinesis mechanisms in developing vertebrate embryos. We have examined cell divisions in two ectodermally-derived tissues of the developing *Xenopus* embryo using 4D confocal microscopy. This analysis has identified striking differences in fundamental mechanism of cell division in the neural plate as compared to tail epidermal cells. The division mechanisms in later epidermal cells reflect those described for differentiated cells in culture. By comparison, cells in the closing neural tube display an exaggerated anaphase B, delayed cytokinesis onset and a pronounced reduction of microtubule density in the spindle midzone. The mechanism of cell division in normal neural plate cells is reminiscent of that observed in cultured cells experimentally depleted of PRC1. We find that PRC1 protein expression is reduced in neural tube cells. Forced expression of PRC1 in neural cells abrogates the extensive spindle elongation and the absence of midzone microtubules. Finally we find that changes in midzone microtubules reflect differences in the midbody. We therefore suggest that the divergent cell division mechanism we observed in neural plate cells may be related to known specializations of the midbody in neural cells These data demonstrate that the central spindle and midbody are developmentally-regulated structures, and reveal unexpected plasticity to fundamental mechanisms of cell division.

doi:10.1016/j.ydbio.2008.05.280

Program/Abstract # 264

Differentiation of trophoblast stem cells into giant cells is triggered by p57 inhibition of CDK1 activity

Matthew J. Kohn [a], Zakir Ullah [a], Rieko Yagi [a], Lyubomir Vassilev [b], Melvin DePamphilis [a]
[a] *Program in Genomics of Development, NICHD, NIH, Bethesda, MD, USA*
[b] *Department of Discovery Oncology, Roche Research Center, Nutley, NJ, USA*

0012-1606/$ – see front matter

Trophoblast giant cells (TGCs) are required for implantation of the embryo into the uterine endometrium. TGCs are one of only two cell types in mammals that are programmed for endoreduplication (multiple rounds of genome duplication without an intervening mitosis). We identified cyclin-dependent kinase 1 (CDK1) as the key regulator of the transition from mitotic cycles to endoreduplication. CDK1 normally promotes entry into mitosis. Specific inactivation of CDK1 using a chemical inhibitor rapidly triggered both endoreduplication and differentiation of trophoblast stem cells (TSCs) into TGCs. In contrast, the same conditions induced abortive endoreduplication in ES cells and MEFs, followed by apoptosis. Normally the transition to TGCs is triggered by FGF4 deprivation, which results in a rapid increase of the CDK-specific inhibitors p21 and p57 with concomitant suppression of CDK1 activity and initiation of endoreduplication. Analysis of gene expression in wild-type, p21−/−, p57−/− and Cdk2−/− TSCs revealed that endoreduplication required p57 and utilized CDK2 under conditions where CDK1 activity was suppressed. Expression of p21 contributed by suppressing synthesis of the G2 checkpoint protein CHK1. These results mark defining stages in the molecular events by which TGCs form and endoreduplication occurs. Furthermore, they also provide mechanistic insight into placentamegaly and pre-eclampsia, a primary cause of premature birth among humans that is associated with p57 deficiency.

doi:10.1016/j.ydbio.2008.05.281

Program/Abstract # 265

Function of a key cell cycle regulator, the CDC25B phosphatase, during neurogenesis

Emilie Peco [a,b], Virginie Sabado [c], François Medevielle [a], Christine Dozier [b], Bernard Ducommun [b], Fabienne Pituello [a]
[a] *Centre de Biologie du Développement, Toulouse, France*
[b] *LBCMCP, Toulouse, France*
[c] *Department of Craniofacial Development, King's College, London, UK*

During spinal cord development, neural progenitors give rise to multiple types of neurons and glia in a stereotyped sequence involving the coordination of cell cycle control, specification and differentiation. In the vertebrate neural tube, Sonic Hedgehog (SHH) known for its role in fate determination also acts on proliferation but the underlying mechanisms remain enigmatic. In this context, we identified a core actor of the G2/M transition, the phosphatase CDC25B, as a target of the SHH/Gli pathway in chick and mouse embryos (Bénazéraf B. et al., Dev. Biol. 2006). By comparing during spinal cord development the dynamic of expression of CDC25B and CDC25A (the other CDC25 family member found in the chicken), we found that *CDC25B*, unlike CDC25A, is not expressed in cycling progenitors of the stem cell zone. Interestingly its expression, initiated ventrally in neural progenitors by SHH/Gli signalling pathway, is concomitant with the onset of neuronal differentiation and later on progresses in correlation with the wave of neurogenesis. We also found that domains co-expressing CDC25A and CDC25B are associated with intense neuronal production. Both observations suggest that adding CDC25B activity specifically favours neurogenic divisions. I am currently analysing the consequences of modifying the combinatorial expression of CDC25A and CDC25B by gain and loss of function experiments on cell cycle kinetics and timing of differentiation. Our recent data will be presented and discussed.

doi:10.1016/j.ydbio.2008.05.282

Program/Abstract # 266

Alterations in HGF/SF-Met signaling in the developing forebrain modulate neuronal proliferation and migration

Gabriela J. Martins [a], Celine Plachez [b], Elizabeth M. Powell [b,c]
[a] *Program in Neuroscience, University of Maryland, Baltimore, USA*
[b] *Department Anatomy and Neurobiology, University of Maryland, Baltimore, USA*
[c] *Department Psychiatry, University of Maryland, Baltimore, USA*

Maturation of the cerebral cortex is dependent on a myriad of critical processes that include proliferation of neurons from the cortical ventricular zone and their radial migration for layer formation. The hepatocyte growth factor/scatter factor (HGF/SF), when bound to its receptor Met, induces a signaling cascade promoting cell movement, proliferation, or differentiation in various cell types. The current study, shows through *in vitro* and *in vivo* assays that neuronal proliferation is HGF/SF dependent. Moreover, we analyzed the importance of HGF/SF-Met signaling on cortical development in a loss-of-function assay via the targeted conditional deletion of Met (Met-fx:Emx1-Cre mouse; whereby the floxed Met allele is rendered null in areas of expression of the Emx1-Cre transcription factor) and a gain-of-function experiment via the over-expression of HGF/SF (RIP-HGF mouse). Neuronal proliferation and migration were analyzed in each transgenic model. The resulting data suggest that Met is required for proper proliferation and migration of neurons as seen by a decrease in cortical thickness and a delay of BrdU-positive cells exiting the proliferative zone of the Met-fx:Emx1-Cre cortex. Conversely, the over-expression of HGF/SF results in an increase in proliferation in the RIP-HGF cortex and altered migration of neuronal subtypes. These results indicate that early perturbations to the HGF/SF-Met signaling system in the forebrain alter critical developmental processes which could lead to long-term cognitive impairments.

doi:10.1016/j.ydbio.2008.05.283

Program/Abstract # 267

Nonmuscle myosin II-B plays important roles in mouse heart development

Xuefei Ma, Robert S. Adelstein
LMC/NHLBI, Bethesda, MD, 20892-1762, USA

Mice ablated for nonmuscle myosin II-B (NM II-B, Myh10) die by E14.5 due to cardiac defects including a marked decrease in the number of cardiac myocytes and double outlet of the right ventricle (DORV) accompanied by a ventricular septal defect. Here we report on the underlying mechanism for these defects. The decrease in cardiac myocytes has two causes: In NM II-B ablated (B^-/B^-) and in II-B hypomorphic mice a decrease in NM II-B results in defective cytokinesis leading to increases in binucleated cardiac myocytes. Interestingly myocyte binucleation (but not myocyte proliferation) can be rescued *in vivo* by a point mutant form of NM II-B (R709C in the myosin heavy chain, B^C/B^C mice) which has a compromised myosin MgATPase activity and cannot propel actin filaments in an *in vitro* motility assay. This, along with other studies, suggests that the role of NM II in cytokinesis is structural rather than dependent on its enzymatic activity. A second cause for decreased myocytes in both B^-/B^- and B^C/B^C hearts is due to defective development of the epicardium and impairment in epicardial FGF signaling. Consistent with defects in function of the epicardium, the B^C/B^C hearts also show abnormal coronary vessel development, with defects in vasculogenesis. Both B^-/B^- mice and B^C/B^C mice also develop a DORV, indicating that both the amount of NM II-B and its motor activity are essential for normal development of the cardiac outflow tract (OFT). This failure in